UA and CT. Full delivery of tPA and heparin was possible in 47 pts. Activated clotting time was >300 sec in all pts. PTCA was performed in 48 pts 20 mins after completion of the infusion. Systemic fibrinogenolysis (fibrinogen pre 408 ± 120 mg/dL, post 398 ± 114) and thrombin activation (no increase in fibrinopeptide A or fragment 1.2) did not occur but prolonged clot lysis was evident (D-Dimer pre 196 ± 179 ng/mL, 4 hours post 849 ± 746, p = 0.0001). Angiographic outcomes were (mean ± SD):

| | Baseline | Post-tPA | Post-PTCA |
|---|---|---|---|
| TIMI Thrombus Scale | 2.2 ± 1.0 | 1.6 ± 1.2** | 0.5 ± 0.9* |
| MLD by QCA (mm) | 0.82 ± 0.42 | 0.89 ± 0.57*** | 1.90 ± 0.59* |
| TIMI Grade Flow | 2.6 ± 0.8 | 2.5 ± 1.0 | 2.9 ± 0.5 |

*p = 0.001, **p = 0.007, ***p = 0.07 (All comparison made with preceding group)

PTCA was successful (<50% residual stenosis) in 87% and 6% had a major bleeding event. In-hospital outcomes were as follows: death 0, myocardial infarction 4%, abrupt reclosure 11%, repeat PTCA 11%, and CABG 6%.

*Conclusion:* Intralesional tPA with intracoronary heparin causes prolonged thrombolysis without thrombin activation and reduces the extent of coronary thrombus in the setting of unstable angina. It is associated with a high PTCA success rate and favorable in-hospital outcome. Further investigations of this method of local adjunctive thrombolysis and PTCA are warranted.

## 1001-26 Local Dissolution of Intracoronary Thrombus with Urokinase Using the Dispatch™ Catheter: Clinical Studies

Joseph F. Mitchel, Daniel B. Fram, Jeffrey A. Hirst, Francis J. Kiernan, Charles Primiano, Adel M. Eldin, David D. Waters, Raymond G. McKay. *Hartford Hospital, University of Connecticut, Hartford, CT*

The Dispatch™ Catheter is a new local drug delivery device which allows for the prolonged infusion of therapeutic agents at an angioplasty site while still maintaining distal coronary perfusion. To determine the efficacy of this device in dissolving intraluminal clot with local urokinase infusion, 29 patients with thrombus-containing stenoses were treated with the Dispatch™ catheter either prior to (n = 16) or following (n = 13) coronary angioplasty or directional atherectomy. The study group consisted of 15 males and 14 females with a mean age of 58.1 years. Clinical diagnoses included unstable angina (n = 14), acute myocardial infarction (n = 11) or post infarction angina (n = 4). Urokinase was infused at either 10,000 unit/cc (n = 22) or 30,000 units/cc (n = 7) at 0.5 cc/min for up to 30 minutes. All coronary angiograms were analyzed to determine Thrombus Score (0–3), TIMI flow, and quantitative coronary measurements pre and post Dispatch™ therapy. (Thrombus Score: 0 = no thrombus, 1 = possible thrombus, 2 = definite thrombus <3 mm, 3 = definite thrombus >3 mm).

*Results:* Infusions of urokinase for 30 mins were well tolerated in 25 patients without adverse clinical, hemodynamic or electrical sequelae. In the remaining 4 patients, limited infusions were tolerated only for 2.5, 5, 6 and 11 mins because of chest pain with EKG changes secondary either to sidebranch occlusion or inadequete distal perfusion. For the entire study group, Thrombus Score decreased from 2.0 ± 0.7 to 0.5 ± 0.8, TIMI Flow increased from 2.1 ± 1.3 to 3.0 ± 0.0, and minimal lumen diameter increased from 0.70 ± 0.59 to 1.58 ± 0.51 mm (all p < 0.01). Distal embolization, no-reflow, and abrupt closure were not observed in any patient.

*Conclusions:* Reduction of thrombus-containing stenoses and dissolution of intracoronary thrombus can be rapidly achieved in patients with infusions of limited quantities of urokinase with the Dispatch™ catheter. Sidebranch occlusion and inability to dilate coronary stenoses with inadequate distal perfusion may limit the duration of drug infusion with this device.

## 1001-27 Rapid Thrombolysis in Experimental Coronary Artery Bypass Grafts

Edward A. Chasteney, P.S. Ravichandran, Deborah Tuke Bahlman, Alan Shearin, Kenton W. Gregory. *Oregon Health Sciences University, Oregon Medical Laser Center, Department of Veterans Affairs Medical Center, Portland, Oregon*

CABG thrombosis is a common disorder without adequate therapy. To assess the effects of selective laser thrombolysis (LT)in CABG, aortocoronary bypasses were created and completely thrombosed in nine swine. Maximal thrombus removal was achieved with pulsed dye laser light (577 nm, 1 μs pulse, 3 Hz, 64 mJ/pulse) by fluid catheter for 6.7 ± 1 min. Graft flow and thrombosis were assessed by angio with global and grafted segment myocardial function measured by epicardial echo at constant load. Mean graft size: 8 mm × 6 cm. Prior to therapy, grafts had no flow (TIMI 0) and complete thrombosis for 60 min. TIMI flow post LT was 2.8 ± 0.4 (p < 0.001) with focal residual mural thrombus. 90 min post LT, graft appearance and flow were unchanged. Wall motion (WM) scored from normal (1) to dyskinetic (4). Index = total WM/14 segments.

| | | Occlusion | 90 min postLT | |
|---|---|---|---|---|
| Global | EF | 0.49 ± 0.09 | 0.55 ± 0.04 | NS |
| | Index | 1.7 ± 0.1 | 1.1 ± 0.1 | (p < 0.05) |
| Grafted Region | Wall Motion | 4 | 1 | (p < 0.01) |
| | %Wall Thick. | −5 | 31 | (p < 0.01) |

*Conclusions:* 1) LT is able to rapidly remove large amounts of thrombus in CABG. 2) Thrombus removal by LT does not cause detectable changes in regional cardiac function. 3) High patency rates persist 90 min. post LT.

## 1001-28 Stenotic Lesions Reliably Form in Porcine Coronary Arteries Using Copper Stents or Intracoronary Heating

Michael E. Staab, Daniel K. Meeker, William D. Edwards, Sanjay S. Srivatsa, Myung Ho Jeong, David R. Holmes Jr., Robert S. Schwartz. *Mayo Clinic and Foundation, Rochester, MN*

The capability of creating stenotic lesions in an animal model is essential to testing new interventional devices. We developed a coronary stenosis model in domestic swine using either heated balloon angioplasty (heat) at high-temperature (80°C for 15 seconds) or copper stents (copper). Animals were sacrificed 14–47 days after artery injury. Morphometric and histologic study of the stenoses created by heat (14 pigs, 33 arteries) and copper (9 pigs, 18 arteries) was performed. Measurement of lumen area and area circumscribed by the internal elastic lamina (IEL) was used to calculate stenosis by 1-(lumen/IEL). Mean stenosis from heat was 66.9 ± 27% and copper 80.7 ± 22%. Stenoses exceeding 50% were produced by heat 78.8% and copper stents 87.5% of the time. Histologically, the heat group was notable for concentric intimal hyperplasia, intact elastic laminae, necrosis of medial cells, calcific deposits in the media, and mild adventitial inflammation and fibrosis. Copper stent lesions demonstrated severe diffuse inflammation, destruction of the elastic laminae, neovascularization, and mild intimal calcification around stent tines.

Percent of Arteries with Histologic Feature

| | Inflammation | | Calcification | | Neovascular | | Fibrosis | | Necrosis | |
|---|---|---|---|---|---|---|---|---|---|---|
| | H | C | H | C | H | C | H | C | H | C |
| Intima | 3% | 90%‡ | 3% | 50%‡ | 3% | 65%‡ | 3% | 50%‡ | 11% | 5% |
| Media | 25% | 95%‡ | 22% | 5% | 11% | 63%‡ | 8% | 74%‡ | 69% | 26%* |
| Adventitia | 69% | 70% | 11% | 5% | 17% | 40%‡ | 64% | 55% | 11% | 5% |

Fisher's Exact Test, two-sided: *p ≤ 0.05, ‡p ≤ 0.0001 H = Heat C = Copper

*Conclusion:* Heated balloon angioplasty or deployment of copper stents into swine coronary arteries reliably creates severe stenoses suitable for testing new interventional devices. Copper stents in particular create very tight and complicated lesions that would challenge new devices. The histopathology differs with copper demonstrating destructive inflammatory lesions vs. orderly intimal hyperplasia and medial calcification observed in heat lesions.

## 1001-29 Prevention of Subacute Stent Thrombosis by Polymer-Polyethylene Oxide-Heparin Coating in the Rabbit Carotid Artery

Sushil Sheth, Vishva Dev, Harvey Jacobs, James S. Forrester, Frank Litvack, Neal L. Eigler. *Cedars-Sinai Medical Center, Los Angeles, CA; University of Utah, Salt Lake City, UT*

Our goals were to develop a rabbit model of subacute stent thrombosis and to evaluate the efficacy of a polymer stent coating with covalently bound heparin for its prevention. Bare metal stents (a nitinol wire coil with 3 stainless steel joints) were implanted in a carotid artery of 10 NZW rabbits with a 3.0 mm balloon catheter, inflated twice at 6 atm for 1 minute. Systemic antiplatelet and antithrombotic therapy was withheld. Animals were sacrificed at 24, 72 and 96 hours. Only the 96 hour group consistently developed occlusive or subocclusive thrombosis. Heparin (0.28 μg/cm$^2$) was linked onto the surface of soluble polymer chains of segmented polyurethaneurea (SPUU) or aliphatic Tecoflex polyurethane membrane (50 μm thick), using polyethylene oxide (PEO) as a hydrophilic spacer group. Eight stents were coated with this polymer-PEO-Heparin coating. Eight bare metal stents and 8 coated stents were deployed in a carotid artery of 16 NZW rabbits. All animals were sacrificed at 96 hours. At the time of sacrifice, both carotids (stented and contralateral nonstented) were exposed and resting blood flow measured. The amount of thrombus on each stent was assessed by a semiquantitative grading scale (I: no lumen encroachment; II: lumen encroachment; III: subocclusive thrombus; IV: occlusive thrombus) and by the weight of the dry thrombus.

*Results:*

| | Carotid Flow (ml/min) | Thrombus Grade (III/IV) | Thrombus Weight (mg) |
|---|---|---|---|
| Bare Stent (N = 8) | 3.8 ± 8.2 | 7 of 8 | 42.2 ± 19.9 |
| Heparin Stent (N = 8) | 21.0 ± 9.2 | 0 of 8 | 6.0 ± 2.4 |
| p-value | 0.0014 | 0.0004 | 0.00016 |

*Conclusions:* The 96 hour rabbit carotid model yields a high frequency of occlusive and subocclusive subacute thrombosis. The stents coated with polymer-PEO-Heparin accumulate significantly less thrombus and have better patency than the uncoated stents at 96 hours in this model of subacute stent thrombosis.

## 1001-30 Comparison of Different Vasodilators on Coronary Flow Reserve in Patients with Documented Coronary Artery Disease

Mun K. Hong, Augusto D. Pichard, S. Chiu Wong, Kenneth M. Kent, Lowell F. Satler, Gaston R. Dussaillant, Ya Chien Chuang, Julie L. MacKenzie, Martin B. Leon. *Washington Hospital Center, Washington, DC*

No-reflow phenomenon after angioplasty or atherectomy may result in important ischemic complications. No-reflow phenomenon is related to distal embolization of microparticulate material and/or spasm in the microcirculation. Maximal vasodilatation of the coronary microcirculation may prevent or terminate episodes of no-reflow phenomenon. In this preliminary study, we evaluated the vasodilatory capacities of agents commonly used during coronary procedures. The coronary flow reserve (CFR = hyperemic/basal flow velocity) was measured with 0.018" Doppler FloWire in coronary arteries with <50% diameter stenoses (6 RCA, 4 LAD, and 10 LCX) in 20 patients (mean age = 64 ± 7 years; 15 men) undergoing angiography (n = 6) or angioplasty (n = 14) in another coronary artery. Random paired CFR measurements in the same artery were obtained with intracoronary adenosine, nitroglycerin (NTG), verapamil, and contrast agents (Hypaque, Hexabrix, and Optiray), with blood injection as a control. After each measurement, basal flow conditions were restored before subsequent test injections. At the doses chosen, there were no hemodynamic or conduction abnormalities, which could influence coronary flow responses.

| | adenosine (6 or 12 μg) | verapamil (100 μg) | verapamil (200 μg) | NTG (50 μg) | NTG (200 μg) | Hypaque (6 ml) | Blood (6 ml) |
|---|---|---|---|---|---|---|---|
| CFR* | 2.2 ± 0.9** | 1.4 ± 0.3 | 1.5 ± 0.3 | 1.7 ± 0.4 | 1.8 ± 0.5 | 2.1± 0.8 | 1.2 ± 0.1 |
| Duration* | 29 ± 9*** | 58 ± 63 | 77 ± 57 | 21 ± 7 | 22 ± 9 | 35 ± 10 | 9 ± 5 |

*p < 0.001 by ANOVA and multiple pairwise comparisons with Bonferroni correction, using adenosine as the comparison group, **p < 0.001 vs. all others except Hypaque, ***p < 0.05 vs. all others except verapamil (100 μg) and Hypaque; Duration of hyperemic response in seconds

Among different contrast agents, there was no difference in CFR, although duration of hyperemia was significantly longer with Hypaque vs. other contrast agents (p < 0.001 by ANOVA). *We conclude* that adenosine and Hypaque had the highest vasodilatory effect among the agents tested. These agents should be further studied for a potential benefit in the prevention or treatment of no-reflow phenomenon during angioplasty and atherectomy procedures.

# 1002 Pediatric Cardiology — Selected Topics

Wednesday, March 22, 1995, Noon–2:00 p.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: Noon–1:00 p.m.

## 1002-83 In Utero Pulmonary Outflow Obstruction: Natural History and Predictors of Postnatal Severity

Lisa K. Hornberger, Philip J. Spevak, Robert W. McDonald, Mary J. Rice, Gerard R. Martin, Stephen P. Sanders, Steven D. Colan, David J. Sahn. *Children's Hospital, Boston, MA; Oregon Health Sci Univ, Portland, OR; Children's National Medical Center, Washington, DC*

We reviewed prenatal and postnatal echocardiograms of fetuses with pulmonary stenosis (PS, n = 14) and pulmonary atresia (PAtr, n = 5), to elucidate the antenatal natural history of PS and PAtr and identify predictors of severe postnatal disease. Fifteen were serially studied *in utero* (age at first study 24 ± 4wks). Fetuses with PS were divided into severe and mild groups according to whether they were (9) or were not (4) ductus-dependent at birth, respectively. Measurements of RV short and long-axis, tricuspid valve, main and branch pulmonary artery (PA) and pulmonary valve dimensions were converted to Z-scores based on age-adjusted normal fetal data. At the initial exam, main and branch PA and pulmonary valve Z-scores were larger in fetuses with mild PS than in those with severe PS or PAtr (p ≤ 0.01). On serial followup, however, growth rates of right heart structures did not differ for mild PS versus severe PS and PAtr groups. Ductal flow *in utero* was antegrade in systole in all with mild PS, but was either bidirectional (5 severe PS) or retrograde only (4 severe PS, all PAtr) in the severe PS and PAtr groups. Initial RV outflow gradients by Doppler did not differ between the mild and severe PS groups with antegrade PA flow (mean 26 ± 12 mmHg). Pulmonary insufficiency was a *consistent* feature in fetuses with mild PS, but was not present in the severe PS or PAtr groups. By color Doppler, 3/4 with mild PS had mild tricuspid regurgitation, whereas mild or moderate tricuspid regurgitation was found in 9/9 with severe PS and 4/5 with PAtr. When severe PS and PAtr groups were compared, there was no significant difference in initial Z-scores or growth rates of right heart structures between the groups. Tricuspid regurgitation severity and initial RV pressure by the tricuspid regurgitation jet (mean 71 ± 21 mmHg) also did not differ between the severe PS and PAtr groups. On serial followup in 6/8 with severe RV outflow obstruction (1 PAtr, 7 severe PS), the RV pressure increased by 18–47 mmHg. In 3/6 serially studied fetuses with antegrade PA flow (2 severe PS, 1 mild PS), the RV outflow gradient increased later in gestation. There was no change in the severity of tricuspid or pulmonary regurgitation during followup in any fetus. The severity of PS may be differentiated *in utero* by the direction of ductal flow, the presence of pulmonary insufficiency, severity of tricuspid insufficiency and the size of the pulmonary valve and PAs. In the absence of antegrade PA flow, severe PS may be difficult to distinguish from PAtr antenatally.

## 1002-84 Three-Dimensional Reconstruction of Atrial Septal Defect from Intracardiac Ultrasound Imaging: Dynamic Shape Change of the Defect in Cardiac Cycle

Kazuyuki Koike, Toshiki Kobayashi, Katsumi Arai, Shunei Kyo, Ryozo Omoto. *Saitama Medical School, Saitama, Japan*

Currently available transcatheter techniques closing atrial septal defect (ASD) are only suitable for small to moderate sized ones. Assessment of the shape and size of ASD as well as their changes in cardiac cycle may be important when transcatheter closure is applied to larger sized defects.

We have developed a three-dimensional reconstruction (3DR) of ASD from images obtained with intracardiac ultrasound (ICUS). Preliminary study disclosed inadequate image quality of ICUS probes with 15 MHz or higher transmission frequency for ASD assessment. Newly developed 10 MHz, 6 Fr. reusable rotating probes was used in this study. ICUS images were obtained from 4 patients with secundum ASD; age 2.3 to 12 years (median 6.5), weight 11.5 to 44 kg (median 19). A 7 Fr. guiding long sheath was introduced from the femoral vein and placed in the superior vena cava. A 6 Fr. ICUS probe was introduced into the long sheath and ECG gated serial ICUS images were obtained through it. Images were recorded on videotape with 1 mm step manual pullback to the inferior vena cava.

The probe was stable in cardiac cycle and the 3DR was achieved with high resolution images. En face view of ASD could be obtained from the both sides of the septum in all patients. Cross-sectional area of the defect (2.47 ± 0.15 $cm^2$) changed significantly in cardiac cycle (4 to 58% larger in systole than in diastole). The largest size of the defect in the cardiac cycle was in endsystole coincided with peak Doppler left to right shunt across the defect. This dynamic shape change of the ASD may have necessitated various conventional transcatheter ASD closure devices double in size to the actual defect.

We concluded that 3DR of ASD from ICUS images can provide important information for the development of new transcatheter ASD closure devices.

## 1002-85 Utility of Unique Projections in Dynamic Transthoracic Three-Dimensional Echocardiography in the Pre- and Post-Operative Delineation of Lesions Associated with Tetralogy of Fallot in Neonates and Infants

Gerald Marx, Michael Vogel, Achi Ludomirski, Lissa Sugeng, Qi-Ling Cao, Alain Delabays, Barbara Romero, David Fulton, Natesa Pandian. *Tufts-New England Medical Center, Boston, MA; Brompton Hospital, London, England; Univ of Michigan, Ann Arbor, Michigan*

Management of tetralogy of Fallot (TOF) is influenced by the size and position of the ventricular septal defects (VSD) and the size and magnitude of infundibular, and pulmonary annular and arterial obwtruction. Three-dimensional (3D) visualization may provide valuable information on these complex lesions and relations to guide gatheter and surgical interventions in TOF. To assess this, we performed 3D Echo (3DE) in 33 neonates and infants with TOF. In 8 pts additional post-operative studies were acquired. Using 5 or 7.5 MHz transducers placed within a rotational or fan-like scanning device positioned on the chest wall or subcostal position, 2DE images were obtained every two degrees over a span of 180 or 90 degrees with ECG and